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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/002,443	01/02/98	SUTTER G	GSF97-06

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DAVID E BROOK
HAMILTON BROOK SMITH & REYNOLDS
TWO MILITIA DRIVE
LEXINGTON MA 02173

EXAMINER	
ZEMAN,M	
ART UNIT	**PAPER NUMBER**
1631	16

DATE MAILED: 12/13/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/002,443	SUTTER ET AL.	
	Examiner	Art Unit	
	Mary Zeman	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *12-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 31-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-52* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claims 1-52 are pending in this application. Claims 12-30 stand withdrawn from consideration as being drawn to a non-elected invention. Claims 35-52 are newly added. New claims 35-52 appear to be directed to the elected invention.

This application contains claims 12-30 drawn to an invention nonelected with traverse in Paper No. 11. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Once any product claims are deemed allowable, Applicant may request the rejoinder of the subject matter of methods of using the elected compositions. Process claims which depend from or otherwise include all the limitations of an allowed product claim and which meet the requirements of 35 U.S.C. 101, 102, 103, and 112 may be entered.

Applicant's arguments filed 9/13/00 have been fully considered but they are not completely persuasive. Any non-reiterated rejections have been withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The filing of these papers obviates the previous rejection under 35 USC 102(a).

Information Disclosure Statement

The IDS, filed 9/18/00, has been considered. An initialed copy of the PTO-1449 is enclosed with this action.

Specification

The amendment filed 12/27/99 remains objected to and the amendment filed 8/18/00 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

"wherein the site of the naturally occurring deletion is not site III" and "wherein the naturally occurring deletion site is selected from the group consisting of: site I, site II, site IV, site V and site VI." Applicant's arguments will be discussed in the below discussion of the new matter rejection, as the arguments are duplicated there in the response.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 1-11 remain rejected and new claims 35-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention..

Claims 1-11 and 35-43 stand rejected as containing new matter, as the new subgenus of deletion sites either a) specifically excluding site III; or b) reciting all sites except site III, do not find basis in the specification as filed. The inventive concepts now being claimed were not set forth in the specification as filed.

The specification, as filed, sets forth that the invention is drawn to MVA viruses having a heterologous antigen inserted into a (any) naturally occurring deletion site of that virus, of which there are six. The specification further sets forth specific examples of inserting heterologous antigens into site II of the MVA virus. Applicant is now claiming a new subgenus of MVA viruses wherein the site is not site III. This new subgenus is not identified as a preferred subgenus in the specification, nor are any particular problems with site III set forth such that one of ordinary skill in the art would reasonably assume that the new subgenus of viruses was intended as the invention.

Applicant argues that the narrowing of the claims to exclude certain embodiments is not necessarily new matter, and cites In re Werthiem in support of those arguments. However, the facts in the instant application can be distinguished from In re Wertheim, and as such, Applicant's conclusions are unpersuasive. In re Wertheim is concerned with concentrations of compounds in a composition, and whether a particular value within a described range is also described. This is different from the instant claims, as the claims are drawn to exclude a specific embodiment from a genus. Further, the court in In re Wertheim notes that their arguments should be limited to the fact pattern of their decision, and distinguished other types of situations:

"We see an important practical distinction between broad generic chemical compound inventions, for example, as in In re Ruschig, supra, in which each compound within the genus is a separate embodiment of the invention, and inventions like that at bar, in which the range of solids content is but one of several process parameters. What those skilled in the art would expect from using 34% solids content in the concentrated extract prior to foaming instead of 35% is a different matter from what those skilled in the art would expect from the next adjacent homolog of a compound whose properties are disclosed in the specification. We wish to make it clear that we are not creating a rule applicable to all description requirement cases involving ranges. "Where it is clear, for instance, that the broad described range pertains to a different invention than the narrower (and subsumed) claimed range, then the broader range does not describe the narrower range. In re Baird, 52 CCPA 1747, 348 F.2d 974, 146 USPQ 579 (1965); In re Draeger, 32 CCPA 1217, 150 F.2d 572, 66 USPQ 247 (1945)." In re Wertheim 191 USPQ 90 (CCPA 1976) at page 98.

It is well settled that Applicant may not claim a specific thing not originally described merely because it comes within the scope of the genus disclosed. (see Ex parte Klager, 132 USPQ 207) Arbitrarily designating a group of materials subgeneric to the group previously claimed which was not delineated or supported as such does not have basis. (see In re Welstead, 174 USPQ 449, 450) (See also In re Ruschig, 154 USPQ 118, 122; In re Smith, 173 USPQ 679, 683; and Ex parte Westphal, 26 USPQ2d 1858, 1860 (BPAI 1993)).

The group originally claimed was the group of recombinant viruses having an insertion in a (any) naturally occurring deletion site of the virus. A specifically disclosed subgenus was the subgenus of MVA viruses having an insertion into the naturally occurring deletion site, site II. The new subgenus of recombinant MVA viruses having an insertion in a naturally occurring deletion site which is not site III is not supported by the original disclosure, nor is the subgenus of recombinant MVA viruses having an insertion in a naturally occurring deletion site selected from I, II, IV, V and VI supported by the original disclosure.

As set forth previously, Claim 1 has been amended to exclude recombinant MVA viruses which have insertions in the site III locus. There is no basis for this negative limitation in the specification, as filed. The specification at page 5 identifies six major deletion loci in the MVA genome, but does not give any basis for the exclusion of insertions into site III. The whole of the specification is directed to recombinant MVA viruses wherein the insertion is at site II. There is no direct teaching that excludes insertions at site III, nor any reasons why one would exclude such insertions. This amendment is new matter, and must be canceled in response to this

rejection. Applicant is reminded that any further amendments should avoid the prior art teachings of insertions into site III without introducing new matter.

Claims 1-5, and 11 remain rejected and new claims 35-38 and 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Small Jr. et al. (US Patent 5,676,950).

Claim 1 is drawn to a recombinant MVA virus having a heterologous insert in one of the naturally occurring deletion sites of MVA, with the caveat that it is not site III. Claim 35 is also drawn to a recombinant MVA virus having a heterologous insert in a naturally occurring deletion site selected from sites I, II and IV-VI.

Applicant argues that Small Jr. et al. do not describe the claimed invention, and Applicant requests particular teachings as to the insertion sites be clearly pointed out. Applicant further argues that Small Jr. does not provide motivation to create the claimed invention, nor is it suggested by Small Jr. These arguments are not persuasive, and will be addressed below.

Small Jr. et al. (US Patent 5,676,950) discloses recombinant MVA viruses wherein antigenic determinants from influenza or from HIV are inserted into a naturally occurring deletion of the MVA virus. MVA is a preferred virus (column 2 lines 29-31), and is disclosed as having six naturally occurring deletion sites in the genome (column 6 lines 14-19). MVA is a preferred virus due to its extreme attenuation, yet unimpaired gene expression (column 6 lines 23-40). This disclosure that heterologous gene expression is unimpaired is a clear indication that MVA viruses having insertions into one of these six deletion sites are able to express that heterologous gene. This disclosure is also a clear suggestion to insert heterologous sequences into the deletion sites of MVA. In fact, that is the thrust of the entire invention of Small Jr. et al. as they are concerned with the expression of influenza antigens from recombinant MVA viruses. Applicant attempts to cast doubt as to where the heterologous sequences of Small Jr. et al. were inserted, but provides no other evidence that those sequences were not inserted into any of the naturally occurring deletion sites. The disclosure and claims of a US Patent have a presumption of validity, absent evidence to the contrary.

Various antigenic sequences to be inserted into the MVA virus genome are contemplated by Small Jr. et al., including hepatitis B antigens (example 4), influenza, measles, diphtheria, tetanus, pertussis, tuberculosis, cholera, and even polysaccharide mimics (column 5 lines 10-28).

The recombinant virus is able to express the foreign gene such that animals vaccinated with the recombinant virus were able to generate a specific immune response to the expressed polypeptide (examples 6-8). The insertion of sequences expressing antigens of HIV proteins into recombinant vaccinia viruses is specifically discussed in Example 4. This is a direct suggestion to create recombinant MVA viruses having heterologous sequences inserted into naturally occurring deletion sites. Small Jr. et al. do not specifically identify which insertion site is used in their recombinant viruses.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have selected any one of the naturally occurring deletion sites of MVA for insertion of sequences encoding heterologous antigens. Small Jr. et al. disclose that MVA has six suitable sites for such insertions, and indicates that any site can be utilized. Heterologous antigens are efficiently expressed from the insertion sites, and such antigens can provide protection from homologous challenge. Small Jr. et al. disclose the suitability of several antigens for such expression, including antigens of viruses, bacteria and parasites. One would have been motivated to use the MVA virus because it is an excellent vaccine candidate due to its extreme attenuation, the availability of insertion sites, the level of gene expression, and the safety for laboratory workers.

Claims 6, 7, 31 and 32, remain rejected and new claims 39, 40, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Small Jr. et al. (US Patent 5,676,950) as applied to claims 1-5, 11, 35-38 and 44-47 above, in view of Altenberger et al. (1989 PTO-1449 AZ) and further in view of Montagnier et al. (US Patent 5,221,610).

The above rejected claims are drawn to recombinant MVA viruses wherein a foreign gene, such as HIV nef, is inserted into a naturally occurring deletion. A preferred deletion site is deletion II.

Small Jr. et al. (US Patent 5,676,950) discloses recombinant MVA viruses wherein antigenic determinants from influenza or from HIV are inserted into a naturally occurring deletion of the MVA virus. MVA is a preferred virus (column 2 lines 29-31), and is disclosed as having six naturally occurring deletion sites in the genome (column 6 lines 14-19). MVA is a preferred virus due to its extreme attenuation, yet unimpaired gene expression (column 6 lines

23-40). This disclosure that heterologous gene expression is unimpaired is a clear indication that MVA viruses having insertions into one of these six deletion sites are able to express that heterologous gene. This disclosure is also a clear suggestion to insert heterologous sequences into the deletion sites of MVA. In fact, that is the thrust of the entire invention of Small Jr. et al. as they are concerned with the expression of influenza antigens from recombinant MVA viruses. Applicant attempts to cast doubt as to where the heterologous sequences of Small Jr. et al. were inserted, but provides no other evidence that those sequences were not inserted into any of the naturally occurring deletion sites. The disclosure and claims of a US Patent have a presumption of validity, absent evidence to the contrary.

Various antigenic sequences to be inserted into the MVA virus genome are contemplated by Small Jr. et al., including hepatitis B antigens (example 4), influenza, measles, diphtheria, tetanus, pertussis, tuberculosis, cholera, and even polysaccharide mimics (column 5 lines 10-28). The recombinant virus is able to express the foreign gene such that animals vaccinated with the recombinant virus were able to generate a specific immune response to the expressed polypeptide (examples 6-8). The insertion of sequences expressing antigens of HIV proteins into recombinant vaccinia viruses is specifically discussed in Example 4. This is a direct suggestion to create recombinant MVA viruses having heterologous sequences inserted into naturally occurring deletion sites. Small Jr. et al. do not specifically identify which insertion site is used in their recombinant viruses, but it is noted that claims 32 and 33 do not specify where the heterologous gene is to be inserted. Those claims are not limited to naturally occurring deletion sites at all, let alone particular sites, and therefore are rendered completely obvious over the teachings set forth in the rejection.

Altenberger et al. (1989) discloses recombinant MVA viruses. Altenberger et al. discloses the location of deletion II, (pages 18-20) and suggests that MVA recombinants can express malaria antigens from genes inserted into this location. (page 25, second paragraph) Altenberger et al. also notes that recombinant MVA viruses having insertions into the deletion II area could potentially be used as vaccines (page 25, last paragraph). Altenberger et al. provides direct suggestion and direct motivation to insert the foreign gene of interest (or any heterologous sequence) into the deletion II region of MVA, in order to obtain foreign gene expression.

Finally, Montagnier et al. (US Patent 5,221,610) discloses the HIV nef protein, and nucleotides encoding nef, for use in producing recombinant nef polypeptides which can be used in HIV detection, and in immunogenic compositions. Montagnier et al. expresses the nef protein from recombinant vaccinia viruses (columns 13 and 14). MVA is a specifically attenuated form of vaccinia virus. Montagnier et al. therefore provide direct motivation to express the nef protein in a vaccinia virus for use in vaccines. These recombinant vaccinia viruses produce a nef polypeptide which is bound by sera from patients with AIDS. Montagnier et al. teaches that recombinant vaccinia viruses can express antigenic nef polypeptides.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have selected any one of the naturally occurring deletion sites of MVA, including site II, for insertion of sequences encoding heterologous antigens. Small Jr. et al. disclose that MVA has six suitable sites for such insertions, and indicate that any site can be utilized. Both Altenberger et al. and Small Jr. et al. disclose that heterologous antigens are efficiently expressed from the insertion sites, and such antigens can provide protection from homologous challenge. Small Jr. et al. disclose the suitability of several antigens for such expression, including antigens of HIV for use in recombinant MVA viruses. One of skill in the art would have been motivated to select the nef gene of HIV in view of the disclosure of Montagnier et al., which indicates that immunogens comprising nef proteins are highly desirable for vaccine compositions against AIDS. One of skill in the art would have been further motivated to use the MVA virus because it is an excellent vaccine candidate due to its extreme attenuation, the availability of insertion sites, the level of gene expression, and the safety for laboratory workers.

Therefore, the invention as a whole is *prima facie* obvious, absent evidence to the contrary.

Claims 6, 7, and 33-34 remain rejected and new claims 39-43 and 48-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Small Jr. et al. (US Patent 5,676,950) as applied to claims 1-5, 11, 35-38 and 44-47 above, in view of Altenberger et al. (1989 PTO-1449 AZ) and further in view of Kwon (US Patent 5,679,511).

The above rejected claims are drawn to recombinant MVA viruses wherein a foreign gene, such as human tyrosinase, is inserted into a naturally occurring deletion. A preferred deletion site is deletion II.

Small Jr. et al. (US Patent 5,676,950) discloses recombinant MVA viruses wherein antigenic determinants from influenza or from HIV are inserted into a naturally occurring deletion of the MVA virus. MVA is a preferred virus (column 2 lines 29-31), and is disclosed as having six naturally occurring deletion sites in the genome (column 6 lines 14-19). MVA is a preferred virus due to its extreme attenuation, yet unimpaired gene expression (column 6 lines 23-40). This disclosure that heterologous gene expression is unimpaired is a clear indication that MVA viruses having insertions into one of these six deletion sites are able to express that heterologous gene. This disclosure is also a clear suggestion to insert heterologous sequences into the deletion sites of MVA. In fact, that is the thrust of the entire invention of Small Jr. et al. as they are concerned with the expression of influenza antigens from recombinant MVA viruses. Applicant attempts to cast doubt as to where the heterologous sequences of Small Jr. et al. were inserted, but provides no other evidence that those sequences were not inserted into any of the naturally occurring deletion sites. The disclosure and claims of a US Patent have a presumption of validity, absent evidence to the contrary.

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Altenberger et al. (1989) discloses recombinant MVA viruses. Altenberger et al. discloses the location of deletion II, (pages 18-20) and suggests that MVA recombinants can express malaria antigens from genes inserted into this location. (page 25, second paragraph) Altenberger et al. also notes that recombinant MVA viruses having insertions into the deletion II area could potentially be used as vaccines (page 25, last paragraph). Altenberger et al. provides direct suggestion and direct motivation to insert the foreign gene of interest (or any heterologous sequence) into the deletion II region of MVA, in order to obtain foreign gene expression.

Finally, Kwon (US Patent 5,679,511) discloses the cDNA sequence encoding human tyrosinase, and the expression of that protein from bacteriophage vectors. Kwon indicates that human tyrosinase is very important for understanding pigment disorders, and cancers such as melanomas. Kwon provides motivation to use the tyrosinase gene as an antigen as it is involved in melanomas, and could be a vaccine antigen.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have selected any one of the naturally occurring deletion sites of MVA, including site II, for insertion of sequences encoding heterologous antigens. Small Jr. et al. disclose that MVA has six suitable sites for such insertions, and indicate that any site can be utilized. Both Altenberger et al. and Small Jr. et al. disclose that heterologous antigens are efficiently expressed from the insertion sites, and such antigens can provide protection from homologous challenge. Small Jr. et al. disclose the use of recombinant MVA viruses for cancer prevention when the proper cancer antigen is provided. Kwon provides that antigen, human tyrosinase, and indicates it could be used in a melanoma vaccine. One of skill in the art would have been further motivated to use the MVA virus because it is an excellent vaccine candidate due to its extreme attenuation, the availability of insertion sites, the level of gene expression, and the safety for laboratory workers.

Therefore, the invention as a whole is *prima facie* obvious, absent evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308 4028.

The fax number for this Art Unit is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center receptionist whose telephone number is (703) 308-0196.

mkz
December 11, 2000

Marianne P. Allen
MARIANNE P. ALLEN
PRIMARY EXAMINER
~~GROUP 1600~~
AU1631